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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/613,762	07/03/2003	Philip Leder	HMV-060.01	7130

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EXAMINER	
ANDERSON, JAMES D	
ART UNIT	PAPER NUMBER
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/613,762	LEDER ET AL.	
	Examiner	Art Unit	
	James D. Anderson	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5-12 and 27-36* is/are pending in the application.

4a) Of the above claim(s) *28 and 30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-12,27,29 and 31-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 9/29/2006, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application. In light of the new rejections being applied against the claims, this Office Action is **Non-Final**.

Change of Examiner

The examiner assigned to the instant application has changed. The new examiner is James D. Anderson, Ph.D. Contact information is provided at the end of this Office Action.

Status of the Claims

Claims 5-12 and 27-36 are currently pending. Claims 28 and 30 are withdrawn, claims 5-7 are presently amended and claims 31-36 are newly presented.

Election/Restrictions

Applicants requested an explanation of why claims 28 and 30 were withdrawn. The previous examiner issued a Restriction Requirement wherein applicants were required to elect a single specie for prosecution. The elected specie is a compound having the formula recited in instant claim 6. Claims 28 and 30 recite compounds wherein R' is H (in the compound recited in

instant claim 5). Thus, the compounds recited in claims 28 and 30 are not drawn to the elected specie and are withdrawn from consideration.

Claim Rejections - 35 USC § 112 (1st Paragraph)

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5-12, 27, 29 and 31-36 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

In the instant case, claims 5-7 recite derivatives, analogs, prodrugs, heterocyclyls, and polycyclyls. There is insufficient written support for these claim limitations in the disclosure.

M.P.E.P. § 2163 states, "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention...one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process."

The terms derivatives, analog and prodrug are extremely broad, encompassing hundreds of thousands of possible compounds. For example, any carbon-containing compound could, in the broadest interpretation, be a "derivative" of the claimed compounds. Further, the structural features of a "prodrug" of the claimed compounds have not been defined. Similarly, applicants define "heterocyclyl" as any 3 to 10-member ring structure having from one to four heteroatoms (page 19). This definition literally encompasses thousands of possible structures. While applicants name a few specific heterocyclyl compounds (*e.g.* page 19), they have provided no description of any methods of synthesizing such a broad sub-genus of compounds. The same is true of the sub-genera of compounds having a "polycyclyl" group. This group of compounds is defined as having "two or more rings" (page 20). However, it is not clear that applicants were in possession of compounds having, for example, 20 rings. The skilled artisan would expect the synthesis of such compounds to be very complex, especially if said ring systems further comprise other substituents. Applicants have provided no description of any methods of synthesizing the claimed compounds having multiple ring systems.

As such, it is not clear that applicants were in possession of the full scope of the claimed compounds at the time the invention was made. Adequate written description requires more than a mere statement that something is part of the invention. In the instant case, it is clear that the skilled artisan could not "immediately envisage" the instantly claimed compounds based on the description provided in the disclosure.

Claims 5-12, 27, 29 and 31-36 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for inhibiting cell proliferation of Neu-initiated

cell lines with F16, does not reasonably provide enablement for inhibiting cell proliferation of any and all cells with the full scope of the claimed compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. This is a Scope of Enablement rejection.

To be enabling, the specification of the patent application must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1561 (Fd. Cir. 1993). Explaining what is meant by "undue experimentation," the Federal Circuit has stated that:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which experimentation should proceed to enable the determination of how to practice a desired embodiment of the claimed invention. PPG v. Guardian, 75 F.3d 1558, 1564 (Fed. Cir. 1996).[1]

The factors that may be considered in determining whether a disclosure would require undue experimentation are set forth by *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 wherein, citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

> 1) the quantity of experimentation necessary,
>
> 2) the amount of direction or guidance provided,
>
> 3) the presence or absence of working examples,

[1] As pointed out by the court in *In re Angstadt*, 537 F.2d 498 at 504 (CCPA 1976), the key word is "undue", not "experimentation".

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art,

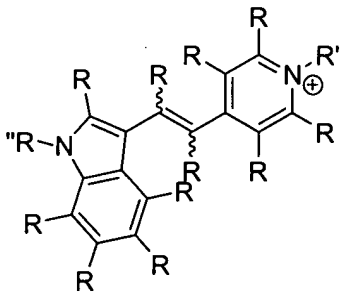
7) the predictability of the art, and

8) The breadth of the claims.

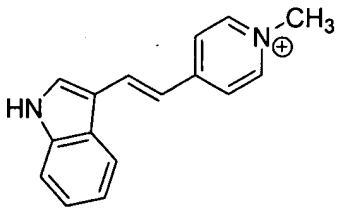
These factors are always applied against the background understanding that scope of enablement varies inversely with the degree of unpredictability involved. *In re Fisher*, 57 CCPA 1099, 1108, 427 F.2d 833, 839, 166 USPQ 18, 24 (1970). Keeping that in mind, the Wands factors are relevant to the instant fact situation for the following reasons:

1. The nature of the invention, state and predictability of the art, and relative skill of those in the art

The invention relates to the inhibition of cell proliferation comprising administering the genus of compounds recited in instant claim 5,



Compounds of claim 5



Compound F16

whereas claim 6 recites a specific compound, F16. The relative skill of those in the art is high, generally that of an M.D. or Ph.D. That factor is outweighed, however, by the unpredictable nature of the art.

As a demonstration of the unpredictability of inhibiting cell proliferation with the claimed compounds, Examiner refers to Example 5 in the specification. In this example, compound F16 was administered to cells derived from Neu, Ras and Myc transgenic mice. It is clear from Table 1 that F16 was ineffective in inhibiting cell proliferation of Ras- and Myc-induced cell lines. As such, it is not evident that the claimed compounds could be predictably used to inhibit cell proliferation of any and all cell lines. Further, it is not evident that compounds with multiple substituents (*e.g.* compounds of claim 5) would be any more effective than an unsubstituted compound (*e.g.* F16).

Clearly, this single example demonstrates that the claimed compounds are not predictable inhibitors of cell proliferation. As such, the skilled artisan would not reasonably expect that the claimed compounds could be used to inhibit cell proliferation of any cell line as instantly claimed.

2. The breadth of the claims

The claims vary in breadth; some (such as claim 5) are extremely broad, reciting the inhibition of cell proliferation by administering a very broad genus of compounds. Others, such as claim 6, are narrower, reciting a single species of the claimed genus of compounds. Dependent claims 31-36 contemplate inhibiting the proliferation of "transformed", "malignant", "benign" and "cancer" cells as well as cells infected "with a virus". All, however, are extremely broad insofar as they disclose the general inhibition of cell proliferation with the same compounds.

3. The amount of direction or guidance provided and the presence or absence of working examples

The specification provides no direction or guidance for determining the particular administration regimes (dosages, timing, administration routes, etc.) necessary to inhibit any and all cell lines with the claimed compounds. The working examples are limited to demonstrating the effects of one specific compound (F16) on a few specific cell lines. Even in this case, only Neu-induced cell lines were effectively and predictably inhibited. No examples are provided demonstrating the inhibition of cell proliferation in benign cells, cells infected with a virus, or any other transformed cells. Thus, the applicant at best has provided specific direction or guidance only for inhibiting the proliferation of Neu-induced cell lines with the compound F16. No reasonably specific guidance is provided concerning useful protocols for any other compounds or cell lines. Further, applicants have not provided any means for the skilled artisan to synthesize the claimed compounds. It is noted that the compounds recited in claim 5 encompass compounds with multiple substituents (13 independent substituents). Clearly, a single generic synthetic protocol cannot be predictably used to synthesize all (or even a reasonable number) of the claimed compounds.

4. The quantity of experimentation necessary

Because of the known unpredictability of the art (as discussed *supra*) and in the absence of experimental evidence commensurate in scope with the claims, the skilled artisan would not accept the assertion that the instantly claimed genus of compounds could be predictably used to inhibit cell proliferation of any and all cell lines as inferred in the claims and contemplated by the specification. Accordingly, the instant claims do not comply with the enablement

requirement of 35 U.S.C. § 112, first paragraph, since to practice the claimed invention a person of ordinary skill in the art would have to engage in undue experimentation, with no assurance of success.

Claim Rejections - 35 USC § 112 (2nd Paragraph)

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 5, 8-12, 27, 29 and 31-36 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In instant claim 5, the definition of R_{80} is unclear or is not defined. It appears a word or space may be missing in the claim, which renders the claim indefinite with respect to the limitations of R_{80}. Claims dependent from claim 5 are included in this rejection.

Claim 31 recites inhibiting the proliferation of "transformed" cells. Aside from cells transformed with an oncogene, it is not clear what other transformed cells are included within this claim limitation. As such, the metes and bounds of this claim limitation are unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 5-7, 27 and 29 are again rejected under 35 U.S.C. § 102(e) as being anticipated by Rondeau *et al.* (US2005/0086748).

Applicant's arguments have been fully considered but are not persuasive. Applicants argue that Rondeau *et al.* disclose administering the claimed compounds to "keratinous fibers", but do not teach, "contacting a cell". However, the skilled artisan would have known that keratinous fibers are composed of cells and that administering a compound to keratinous fibers will inherently contact said cells. As such, the rejection of claims 5-7, 27 and 29 is maintained and reiterated below.

The instant claims recite a method of inhibiting cell proliferation by contacting a cell with a compound as recited in claim 5. No limitations are recited with respect to the type of cell being contacted.

Rondeau *et al.* recite a method of dyeing keratinous fibers by contacting the keratinous fibers with compounds encompassed by the instant claims (Abstract and ¶ [0086]). The claims are anticipated because Rondeau *et al.* disclose contacting a cell(s), *i.e.* cells of the hair and scalp, with a composition containing the identically claimed compound using the claimed method steps. Accordingly, inhibition of the proliferation or stimulation of differentiation or induction of cell death of the cell(s) would be inherent. Further, it is noted that the instant application contemplates the application of the instant compounds to the hair in order to reduce the growth of human hair (page 48). *In re Best* (195 USPQ 430) and *In re Fitzgerald* (205 USPQ 594) discuss the support of rejections wherein the prior art discloses subject matter, which there is reason to believe inherently includes functions that are newly cited, or is identical to a product

instantly claimed. In such a situation the burden is shifted to the applicants to "prove that subject matter to be shown in the prior art does not possess the characteristic relied on" (205 USPQ 594, second column, first full paragraph). There is no requirement that a person of ordinary skill in the art would have recognized the inherent disclosure at the time of invention, but only that the subject matter is in fact inherent in the prior art reference. *Schering Corp. v. Geneva Pharm. Inc.*, 339 F.3d 1373, 1377, 67 USPQ2d 1664, 1668 (Fed. Cir. 2003); see also *Toro Co. v. Deere & Co.*, 355 F.3d 1313, 1320, 69 USPQ2d 1584, 1590 (Fed. Cir. 2004) ("[T]he fact that a characteristic is a necessary feature or result of a prior-art embodiment (that is itself sufficiently described and enabled) is enough for inherent anticipation, even if that fact was unknown at the time of the prior invention").

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James D. Anderson whose telephone number is 571-272-9038. The examiner can normally be reached on MON-FRI 9:00 am - 5:00 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

James D. Anderson, Ph.D.
Patent Examiner
AU 1614

Phyllis Spivack
1/29/07

January 29, 2007

PHYLLIS SPIVACK
PRIMARY EXAMINER